



KAREN L. SMITH, MD, MPH
Director and State Public Health Officer

State of California—Health and Human Services Agency
California Department of Public Health



EDMUND G. BROWN JR.
Governor

May 25, 2016

Dear STD Prevention Colleagues:

Bicillin® L-A (Benzathine Penicillin G) Shortage

On April 29, 2016, a Bicillin® L-A (penicillin G benzathine suspension) drug shortage was announced by the Food and Drug Administration (FDA). There are manufacturing delays in both adult and pediatric injections; the back order is expected to resolve by July 2016. This is of concern because California is in the midst of very significant increases in syphilis, including syphilis in pregnant women and congenital syphilis in infants. **Benzathine penicillin G is the recommended treatment for syphilis, and the only recommended treatment for pregnant women with syphilis.** Treatment of syphilis in pregnancy is nearly 100% effective at preventing the potentially devastating outcomes associated with congenital syphilis, including long term morbidity and stillbirths, but it needs to be administered promptly and correctly.

In light of the shortage of Bicillin® L-A, the California Department of Public Health (CDPH) STD Control Branch (STDCB) recommends the following:

- 1) STD Controllers should notify health care providers in local health jurisdictions who are diagnosing and treating syphilis on site. Communication about the drug shortage should include:
 - a. Information about the Bicillin® L-A shortage and the expected end date of July 2016, and include the links to the:
 - i. FDA website announcing the Bicillin® L-A shortage:
[http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillin%20G%20Benzathine%20\(Bicillin%20L-A\)%20Injection&st=c&tab=tabs-1](http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillin%20G%20Benzathine%20(Bicillin%20L-A)%20Injection&st=c&tab=tabs-1).
 - ii. CDC notice about the Bicillin® L-A shortage:
<http://www.cdc.gov/std/treatment/drugnotices/bicillinshortage.htm>.
 - b. The recommended treatment regimens for syphilis and the link to the CDC STD Treatment Guidelines for syphilis:
<http://www.cdc.gov/std/tg2015/syphilis.htm>.



- c. Information about doxycycline as an alternative treatment for syphilis, including that:
 - i. Doxycycline is contraindicated in pregnant women and young children.
 - ii. The dose for doxycycline is 100mg orally twice a day for 14 days for primary, secondary, and early latent syphilis, and 100mg orally twice a day for 28 days for late latent syphilis.
 - iii. Follow-up clinical and serologic evaluation should be performed after treatment at the recommended intervals per the CDC STD Treatment Guidelines.
 - d. That other formulations of penicillin, including Bicillin® C-R, are not acceptable alternatives to Bicillin® L-A for syphilis treatment.
 - e. That use of benzathine penicillin G should be discouraged for the treatment of other infectious diseases (e.g., streptococcal pharyngitis) where other effective antimicrobials are available.
 - f. That adherence to the recommended dosing regimen of 2.4 million units of benzathine penicillin G intramuscular (IM) for the treatment of primary, secondary, and early latent syphilis should be encouraged; additional doses to treat early syphilis do not enhance efficacy including in patients living with HIV infection.
 - g. Any local recommendations for prioritization of Bicillin® L-A; see #3 below for considerations.
 - h. Local contact number for health care providers with questions or who need assistance in obtaining Bicillin® L-A.
- 2) STD Controllers should assess local inventory (including public health and high-morbidity private health care providers' inventory), review local epidemiology, and estimate needs over the next two months based on syphilis trends. The CDPH STDCB currently has very limited inventory of Bicillin® L-A, and is attempting to place additional orders.
- a. If you have a critical shortage of Bicillin® L-A or if one of your community health care providers has a critical shortage, or if you have a surplus that could be shared with other health care providers, please contact ashley.williamson@cdph.ca.gov in the STD Control Branch.
- 3) If your local health jurisdiction needs to prioritize doses and implement a usage strategy based on assessment of local Bicillin® L-A inventory, considerations for prioritization include:

- a. Benzathine penicillin G is the only recommended treatment for pregnant women infected or exposed to syphilis. There are no alternatives.
- b. Primary and secondary syphilis are the most infectious stages. Treatment is necessary to interrupt transmission.
- c. Patients with early latent syphilis and patients with latent syphilis of unknown duration with high titers should be considered potentially able to transmit syphilis.
- d. Complications of syphilis, including neurosyphilis and ocular syphilis, can occur at any stage, thus it is important to ensure complete and appropriate treatment of all patients with syphilis.
- e. Persons with HIV infection who have early syphilis might be at increased risk for neurologic complications.
- f. Benzathine penicillin G has the benefit of directly observed therapy and is not reliant on patient adherence to a 14- or 28-day regimen of twice-daily doxycycline, and therefore benzathine penicillin G is ideal for those in whom medication compliance or follow-up may be in question. Additionally, patients with contraindications to doxycycline should be considered priorities for benzathine penicillin G administration.
- g. Presumptive treatment of sex partners of patients with syphilis remains a high priority and should be managed per the CDC STD Treatment Guidelines. Choice regarding use of Bicillin® L-A versus doxycycline should be made after considering likelihood of medication adherence, patient follow-up, and local availability of Bicillin® L-A.

We will keep you updated as we learn more about the drug shortage.

For clinical questions related to the treatment of syphilis during the Bicillin® L-A shortage, please contact the CDPH STDCB Clinician Warm Line at (510) 620-3400 or submit an online consult to the STD Clinical Consultation Network at www.stdccn.org.

Sincerely,



Heidi Bauer, MD, MPH, MS
Chief, STD Control Branch
California Department of Public Health
Office: (510) 620-3178
Heidi.Bauer@cdph.ca.gov
www.std.ca.gov